Amendments to the Claims

1-28. (Cancelled)

29. (Currently Amended) A method for producing a ~~genetically modified lymphoid cell capable of directed and selective genetic diversification of a~~ hypermutated transgenic target nucleic acid sequence ~~by hypermutation~~ comprising

a) transfecting a lymphoid cell with a genetic construct comprising ~~said~~ a target nucleic acid sequence;

b) integrating said target nucleic acid sequence into the immunoglobulin locus of said lymphoid cell ~~to produce said genetically modified lymphoid cell~~, wherein said lymphoid cell is a B cell from a chicken, sheep, cow, pig or rabbit with a functional activation-induced deaminase (AID) protein and contains no deleterious mutations in genes encoding XRCC2, XRCC3, or RAD51 proteins or their analogues; and

c) producing said hypermutated transgenic target nucleic acid sequence~~, said lymphoid cell is capable of gene conversion prior to transfection, and said hypermutation in said genetically modified lymphoid cell occurs at a rate higher than the background mutation rate in said lymphoid cell~~.

30. (Withdrawn) The method according to claim 29, wherein said genetic construct further comprises a nucleic acid sequence capable of serving as a gene conversion donor for said target nucleic acid sequence.

31-34. (Cancelled)

35. (Currently Amended) The method according to claim 29, wherein ~~transfecting said lymphoid cell comprises inserting~~ said integrating said target nucleic acid sequence into said immunoglobulin locus of said lymphoid cell is by targeted integration.

36-43. (Cancelled)

44. (Currently Amended) The method according to claim 29, wherein an endogenous V-gene segment or a fragment thereof in said lymphoid cell is replaced with said target nucleic acid sequence.

45. (Previously Presented) The method according to claim 29, wherein said lymphoid cell is capable of homologous recombination and DNA repair.

46. (Previously Presented) The method according to claim 29, wherein said lymphoid cell is an immunoglobulin-expressing B cell.

47. (Canceled)

48. (Previously Presented) The method according to claim 29, wherein said lymphoid cell is a chicken Bursal lymphoma cell.

49. (Previously Presented) The method according to claim 29, wherein said lymphoid cell is a DT40 cell or a derivative thereof.

50. (Previously Presented) The method according to claim 29, wherein said target nucleic acid sequence encodes a protein or expresses a regulatory activity.

51. (Currently Amended) The method according to claim 29, wherein said target nucleic acid sequence encodes a protein selected from the group consisting of an immunoglobulin chain, a selection marker, a DNA-binding protein, a DNA-binding protein fragment, an enzyme, a receptor protein, and a receptor protein fragment.

52. (Currently Amended) The method according to claim 29, wherein said target nucleic acid sequence is a human immunoglobulin V-gene segment or a part thereof.

53. (Previously Presented) The method according to claim 29, wherein said target nucleic acid sequence comprises a transcription regulatory element or an interfering RNA (RNAi) sequence.

54. (Previously Presented) The method according to claim 53, wherein said transcription regulatory element is a promoter.

55. (Currently Amended) The method according to claim 29, further comprising (d) identifying said ~~genetically modified~~ lymphoid cell containing said hypermutated transgenic target nucleic acid sequence.

56. (Currently Amended) The method according to claim 55, wherein said identifying said ~~genetically modified~~ lymphoid cell containing said hypermutated transgenic target nucleic acid sequence comprises identifying a protein encoded by said hypermutated transgenic target nucleic acid sequence on the surface of said ~~genetically modified~~ lymphoid cell, within said ~~genetically modified~~ lymphoid cell, or outside of said ~~genetically modified~~ lymphoid cell.

57. (Withdrawn and Currently Amended) The method according to claim 30, further comprising modulating ~~said selective genetic diversification~~hypermutation of said transgenic target nucleic acid sequence by varying the number, the orientation, the length or the degree of homology of said nucleic acid sequence capable of serving as a gene conversion donor.

58. (Currently Amended) The method according to claim 29, further comprising modulating ~~said selective genetic diversification~~hypermutation of said transgenic target nucleic acid sequence with a DNA repair or recombination factor other than a XRCC2, XRCC3, or RAD51 protein[[s]] or their analogue[[s]].

59. (Previously Presented) The method according to claim 58, wherein said DNA repair or recombination factor is a RAD54 protein.

60-62. (Canceled)

63. (Currently Amended) The method according to claim 29, wherein said lymphoid cell ~~comprises a functional AID protein and~~ has no pseudo-V gene[[s]] segment.

64. (Canceled)

65. (Currently Amended) The method according to claim 29, wherein ~~said~~ hypermutation is at a rate above an order of 10^{-9} to 10^{-10} bp^{-1} $generation^{-1}$.

66. (Canceled)

67. (Currently Amended) The method according to claim 29, wherein ~~said~~ hypermutation is at a rate between 10^{-5} to 10^{-3} bp^{-1} $generation^{-1}$.

68. (Canceled)

69. (Canceled)

70. (Canceled)

71. (Canceled)

72. (Previously Presented) The method of claim 29, wherein said transgenic target nucleic acid sequence is in the absence of an adjacent donor sequence capable of serving as a gene conversion donor for said transgenic target nucleic acid sequence.

73. (Canceled)

74. (New) The method according to claim 55, wherein a gene product of said hypermutated nucleic acid sequence has an optimized desired activity.

75. (New) The method according to claim 55, wherein said identifying further comprises (e) culturing said lymphoid cell under appropriate conditions to express a mutated gene product encoded by said hypermutated transgenic target nucleic acid sequence; (f) identifying said cultured cell that expresses said mutated gene product having a desired activity; (g) establishing a clonal population of cells from said cultured cell; and (h) selecting from said clonal population a cell that expresses a gene product of said hypermutated transgenic target nucleic acid sequence having an improved desired activity.

76. (New) The method according to claim 75, wherein steps (f) through (h) are iteratively repeated.

77. (New) The method according to claim 75, further comprising switching off hypermutation.

78. (New) The method according to claim 77, wherein said hypermutation is switched off by down-regulation of the expression of a *trans*-acting regulatory factor.

79. (New) The method according to claim 78, wherein said *trans*-acting regulatory factor is activation-induced deaminase (AID).